
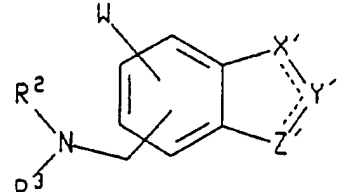


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(21) International Application Number: PCT/US93/09407 (22) International Filing Date: 7 October 1993 (07.10.93) (30) Priority Data: 07/988,653 10 December 1992 (10.12.92) US (60) Parent Application or Grant (63) Related by Continuation US 07/988,653 (CIP) Filed on 10 December 1992 (10.12.92) (71) Applicant (for all designated States except US): PFIZER INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): HOWARD, Harry, R. [US/US]; 272 Westwoods Terrace, Bristol, CT 06010 (US). O'NEILL, Brian, T. [US/US]; 1526 Essex Road, Westbrook, CT 06498 (US). (74) Agents: RICHARDSON, Peter et al.; Pfizer Inc., 4G235 East 42nd Street, New York, NY 10017 (US).		(81) Designated States: AU, CA, JP, KR, NO, NZ, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published With international search report.
(54) Title: AMINOMETHYLENE SUBSTITUTED NON-AROMATIC HETEROCYCLES AND USE AS SUBSTANCE P ANTAGONISTS		
<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>(Ia)</p> </div> <div style="text-align: center;">  <p>(Ib)</p> </div> </div>		
(57) Abstract <p>The present invention relates to novel aminomethylene substituted non-aromatic heterocycles and, specifically, to compounds of formula (Ia) or (Ib) wherein W, R¹, R², R³, A, X', Y' and Z' are as defined in the specification, and to intermediates used in the synthesis of such compounds. The novel compounds of formulae (Ia) and (Ib) are useful in the treatment of inflammatory and central nervous system disorders, as well as other disorders.</p>		

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phase was dried and evaporated (9.9 grams). This material was used without further purification.

Mass Spectrum m/e 181 (m+)

C. Methyl-2-methoxy-5-benzamidobenzoate

5 A solution of 9.92 grams (55 mmol) of methyl-2-methoxy-5-aminobenzoate was taken up in 250 ml methylene chloride, treated with 8.4 mL (61 mmol) triethylamine and cooled to 0°C. The reaction mixture was then treated with 8.1 grams (57 mmol) benzoyl chloride in a dropwise fashion. The
10 reaction mixture was stirred for 30 minutes while warming to room temperature. The reaction mixture was diluted with 500 mL of methylene chloride, washed with 200 mL saturated bicarbonate solution and then rewashed with water and brine. The organic phase was dried and evaporated to a flaky white
15 solid (15.7 grams). This material was used without further purification.

Mass Spectrum: m/e 286 (m+1)

D. Methyl-2-methoxy-5-benzthioamido-benzoate

A 2 liter round bottom flask was charged with 15.7
20 grams (55 mmol) methyl-2-methoxy-5-benzamidobenzoate and 22.2 grams (55 mmol) of Lawesson's reagent followed by 500 mL of toluene. The reaction mixture was heated under reflux for 1.5 hours. The mixture was diluted with 500 mL of ethyl acetate, and washed with 250 mL of saturated aqueous
25 bicarbonate solution, followed by washes with water and brine. The organic layer was dried over sodium sulfate, filtered and evaporated. The residue was chromatographed on silica eluting with 96/4 methylene chloride - ether. There was obtained 14.8 grams (89%) of desired material.

30 E. Methyl-6-methoxy-2-phenyl-5-benzothiazolcarboxylate

A 2 liter round bottom flask was charged with 81 grams (246 mmol) potassium ferricyanide in 300 mL of water, the solution was warmed to 55°C. A solution of 14.78 grams (49
35 mmol) methyl-2-methoxy-5-benzthioamido-benzoate in 200 mL of methanol and 100 mL aqueous sodium hydroxide solution [13.7 gm (343 mmol) NaOH/100 mL] was then added. A yellow